Clinical trials of ximelagatran

TrialResults-center www.trialresultscenter.org

1 atrial fibrillation

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<tr>
<th>Trial</th>
<th>Treatments</th>
<th>Patients</th>
<th>Trials design and methods</th>
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<tr>
<td>ximelagatran vs warfarin standard dose</td>
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<tr>
<td><strong>SPORTIF V, 2005</strong></td>
<td>ximelegatran 36 mg twice daily</td>
<td>One or more stroke risk factor in addition to atrial fibrillation.High risk patients with non valvular atrial fibrillation.</td>
<td>Parallel groups</td>
</tr>
<tr>
<td>n=1960/1962</td>
<td>versus warfarin standard dose (target INR 2-3)</td>
<td></td>
<td>Double blind</td>
</tr>
<tr>
<td>follow-up: 20 months</td>
<td></td>
<td></td>
<td>north america</td>
</tr>
<tr>
<td><strong>SPORTIF II (ximelagatran vs warfarin standard dose) , 2002</strong></td>
<td>ximelegatran 20,40,60 mg twice daily versus warfarin standard dose (target INR 2-3)</td>
<td>Medium to high risk patients with chronic non valvular atrial fibrillation.</td>
<td>Parallel groups</td>
</tr>
<tr>
<td>n=187/67</td>
<td></td>
<td></td>
<td>Open</td>
</tr>
<tr>
<td>follow-up: 16 weeks</td>
<td></td>
<td></td>
<td>Europe ,USA</td>
</tr>
<tr>
<td><strong>SPORTIF III, 2003</strong></td>
<td>ximelegatran 36 mg twice daily</td>
<td>One or more stroke risk factor in addition to AF.High risk patients with non valvular atrial fibrillation.</td>
<td>Parallel groups</td>
</tr>
<tr>
<td>n=1704/1703</td>
<td>versus warfarin standard dose (target INR 2-3)</td>
<td></td>
<td>Open</td>
</tr>
<tr>
<td>follow-up: 17.4 months</td>
<td></td>
<td></td>
<td>europe,asia,australasia</td>
</tr>
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</table>

More details and results:

- antithrombotics for atrial fibrillation in primary prevention of thromboembolic events at http://www.trialresultscenter.org/go-Q57
- direct antithrombins for atrial fibrillation in all type of patients at http://www.trialresultscenter.org/go-Q368
- direct oral anticoagulant (DAO) for atrial fibrillation in all type of patients at http://www.trialresultscenter.org/go-Q391

References

SPORTIF V, 2005:
Halperin JL Ximelagatran compared with warfarin for prevention of thromboembolism in patients with nonvalvular atrial fibrillation: Rationale, objectives, and design of a pair of clinical studies and baseline patient characteristics (SPORTIF III and V). Am Heart J 2003 Sep;146:431-8 [12947359]

SPORTIF II (ximelagatran vs warfarin standard dose), 2002:

SPORTIF III, 2003:

2 acute coronary syndrome

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<tr>
<td>ESTEEM, 2003</td>
<td>Oral ximelagatran at doses of 24 mg, 36 mg, 48 mg, or 60 mg twice daily versus placebo</td>
<td>Patients who had had recent ST-elevation or non-ST elevation myocardial infarction</td>
<td>Parallel groups double-blind</td>
</tr>
</tbody>
</table>

More details and results:
- antithrombotics for acute coronary syndrome in all type of patients at [http://www.trialresultscenter.org/go-Q24](http://www.trialresultscenter.org/go-Q24)
- anticoagulant for acute coronary syndrome in all ACS (including AMI) at [http://www.trialresultscenter.org/go-Q167](http://www.trialresultscenter.org/go-Q167)
- direct factor Xa inhibitors for acute coronary syndrome in all type of patients at [http://www.trialresultscenter.org/go-Q345](http://www.trialresultscenter.org/go-Q345)
- direct oral anticoagulant (DAO) for acute coronary syndrome in all type of patients at [http://www.trialresultscenter.org/go-Q480](http://www.trialresultscenter.org/go-Q480)

References

ESTEEM, 2003:

3 thrombosis prevention
## Trial Treatments Patients Trials design and methods

### ximelagatran vs Dalteparin

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<tbody>
<tr>
<td>METHRO I, 2002</td>
<td>Melagatran 14 mg s.c. immediately before surgery, melagatran at 20:00 hours, then ximelagatran 624 mg orally b.d. for 69 days versus Dalteparin 5000 IU o.d., started evening before surgery for 69 days</td>
<td>adults undergoing hip or knee replacement</td>
<td>parallel group open Swedish</td>
</tr>
<tr>
<td>n=103, follow-up: 69 days</td>
<td></td>
<td></td>
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<tr>
<td>METHRO II, 2002</td>
<td>Melagatran 13 mg s.c. immediately before surgery, melagatran same day, then ximelagatran 824 mg orally b.d. for 710 days versus Dalteparin 5000 IU o.d., started evening before surgery for 710 days</td>
<td>undergoing hip or knee replacement</td>
<td>Parallel groups double-blind</td>
</tr>
<tr>
<td>n=1495/381, follow-up: 710 days</td>
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### ximelagatran vs Enoxaparin

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<tbody>
<tr>
<td>Platinum (Colwell), 2003</td>
<td>Ximelagatran 24 mg orally b.d., starting at least 12 h after surgery for 712 days versus Enoxaparin 30 mg s.c. b.d., starting at least 12 h after surgery for 712 days</td>
<td>adults undergoing hip replacement</td>
<td>parallel group double-blind USA, Canada, Israel, Mexico, Argentina, South Africa</td>
</tr>
<tr>
<td>n=906/910, follow-up: 712 days</td>
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<td></td>
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<tr>
<td>METHRO III, 2002</td>
<td>Melagatran 3 mg s.c. 412h after surgery, then ximelagatran 24 mg orally b.d. for 710 days versus Enoxaparin 40 mg s.c. o.d. 12 h before surgery for 710 days</td>
<td>hip or knee replacement</td>
<td>double-blind Europe, South Africa</td>
</tr>
<tr>
<td>n=2788, follow-up: 811 days</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Phase II (Heit), 2001</td>
<td>Ximelagatran 8, 12, 18 or 24 mg orally b.d., at least 12 h after surgery for 612 days versus Enoxaparin 30 mg s.c. b.d., starting at least 12 h after surgery for 612 days</td>
<td>adults (age&gt;18 years and weight at least 40 kg) undergoing knee replacements</td>
<td>parallel group double-blind North American</td>
</tr>
<tr>
<td>n=600, follow-up: 612 days</td>
<td></td>
<td></td>
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<tr>
<td>EXPRESS, 2003</td>
<td>Melagatran 2 mg s.c. up to 30 min before surgery, then melagatran 3 mg at least 8 hafter surgery, then ximelagatran 24 mg orally b.d. for 811 days versus Enoxaparin 40 mg s.c. o.d., starting 12 h before surgery for 811 days</td>
<td>hip or knee replacement</td>
<td>parallel group double-blind Europe</td>
</tr>
<tr>
<td>n=2835, follow-up: 811 days</td>
<td></td>
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</tbody>
</table>

More details and results:
- antithrombotics for thrombosis prevention in orthopedic surgery at http://www.trialresultscenter.org/go-Q37
- antithrombotics for thrombosis prevention in elective major knee surgery at http://www.trialresultscenter.org/go-Q38
- direct antithrombins for thrombosis prevention in orthopedic surgery at http://www.trialresultscenter.org/go-Q185

References

**METHRO I, 2002:**

**METHRO II, 2002:**

**Platinum (Colwell), 2003:**

**METHRO III, 2002:**

**Phase II (Heit), 2001:**

**EXPRESS, 2003:**
## 4 venous thrombosis

<table>
<thead>
<tr>
<th>Trial</th>
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</tr>
</thead>
</table>
| **ximelagatran vs discontinuation**  
THRIVE III, 2003 | ximelagatran 24 mg twice daily for 18 months versus placebo for 18 months | patients with venous thromboembolism who had undergone six months of anticoagulant therapy | Parallel groups double blind 18 countries |
| n=612/611  
follow-up: 18 months | | | |
| **ximelagatran vs placebo**  
Schulman (subgroup), 2003 | extended treatment with Ximelagatran 24 mg twice daily after initial anticoagulant treatment for 6 months versus placebo (initial anticoagulant treatment for 6 months) | study subgroup of patients with active cancer in the previous 5 years treated for DVT or pulmonary embolism for 6 months without recurrence | Parallel groups single blind and outcome ass. |
| n=NA  
follow-up: 18 months | | | |
| **THRIVE 3, 2003**  
imelagatran (24 mg) versus placebo | patients with venous thromboembolism who had undergone six months of anticoagulant therapy | | |
| n=612/611  
follow-up: | | | |
| **ximelagatran vs LMWH/VKA**  
Fiessinger, 2005 | ximelagatran 36 mg twice daily versus subcutaneous enoxaparin, 1 mg/kg twice daily, for 5 to 20 days followed by warfarin adjusted to maintain an international normalized ratio of 2.0 to 3.0. | patients with acute deep vein thrombosis | double blind |
| n=NA  
follow-up: | | | |
| **ximelagatran (without LMWH) vs LMWH/VKA**  
THRIVE 1, 2003 | oral ximelagatran (24, 36, 48 or 60 mg twice daily) for 2 weeks versus dalteparin and warfarin for 2 weeks | Patients with acute DVT | | |
| n=NA  
follow-up: | | | |

More details and results:

- antithrombotics for venous thrombosis in all type of patients at [http://www.trialresultscenter.org/go-Q101](http://www.trialresultscenter.org/go-Q101)
- direct factor Xa inhibitors for venous thrombosis in all type of patients at [http://www.trialresultscenter.org/go-Q372](http://www.trialresultscenter.org/go-Q372)
• direct oral anticoagulant (DAO) for venous thrombosis in all types of patients at http://www.trialresultscenter.org/go-Q505
• antithrombotics for venous thrombosis in secondary prevention - 2 at http://www.trialresultscenter.org/go-Q682

References

THRIVE III, 2003:

Schulman (subgroup), 2003:

THRIVE 3, 2003:

Fiessinger, 2005:

THRIVE I, 2003:

Entry terms: ximelagatran, xi-melagatran, Exanta, H 376 95, H 376-95,